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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/673,341	10/13/2000	Hisakazu Kurita	K0448/7003	5123

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EXAMINER	
GHALI, ISIS A D	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 05/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/673,341	KURITA ET AL.	
	Examiner	Art Unit	
	Isis Ghali	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 February 2005* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-6,11 and 12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-6, 11 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The receipt is acknowledged of applicants' amendment filed 02/03/2005.

Claims 2 and 7-10 have been canceled.

Claims 1, 3-6, 11 and 12 are pending and included in the prosecution.

Claim Rejections - 35 USC § 103

1. Claims 1, 3-6, 11 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over JP 08-157365 ('365).

JP '365 teaches a transdermal adhesive preparation having remarkable high skin permeation rate and remarkable reduced skin irritation and provides good medicine stability. The preparation comprising 0.1-10 wt.% base drug salt and 0.5-5 wt.% of sodium acetate (abstract; page 1 of the translation, claim 6; page 3, paragraph 009).

The reference does not expressly disclose the organic acid in the powder from or the mean diameter of the powder particles.

However, in the examples pages 6 and 7, paragraphs 0029- 0031, the reference disclosed the components are dissolved except for the sodium acetate, and this suggests the powder form of the sodium acetate. Further the reference disclosed in the same examples that the thickness of the adhesive film that contains the components is

50-100 micrometers, and this implies that the particles size of the powdered organic acid cannot be more than 100 micrometers in diameter.

Thus, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide a transdermal adhesive preparation comprising active agent and sodium acetate powder as disclosed by JP '365, and select the sodium acetate having particles size less than 50 micrometers as suggested by the reference, motivated by the teaching of the reference that such preparation has remarkable high skin permeation rate and remarkable reduced skin irritation and provides good medicine stability, with reasonable expectation of having stable transdermal preparation with the contained sodium acetate particles having diameters less than 50 micrometers with high skin permeability rates and reduced skin irritation.

2. Claims 1, 3-6, 11 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over JP 10045570 ('570).

JP '570 teaches percutaneous adhesive preparation that has low skin irritation and excellent skin permeability (abstract). The preparation comprises 0.05 wt.% of active agent and 0.01-15 wt.% of sodium acetate (abstract; claims 1, 2; page 2, 0006, 0008).

The reference does not expressly disclose the organic acid in the powder from or the mean diameter of the powder particles.

However, in the examples page 5, paragraphs 0019- 0021, the reference disclosed the components are dissolved except for the sodium acetate, and this

suggests the powder form of the sodium acetate. Further the reference disclosed in the same examples that the thickness of the adhesive film that contains the components is 50-100 micrometers, and this implies that the particles size of the powdered organic acid cannot be more than 100 micrometers in diameter.

Thus, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide a transdermal adhesive preparation comprising active agent and sodium acetate powder as disclosed by JP '570, and select the sodium acetate having particles size less than 50 micrometers as suggested by the reference, motivated by the teaching of the reference that such a preparation has low skin irritation and excellent skin permeability, with reasonable expectation of having transdermal preparation with the contained sodium acetate particles having diameters less than 50 micrometers that highly permeates the skin with minimum irritation.

3. Claims 1, 3-6, 11 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,866,157 ('157).

US '157 teaches an adhesive composition for matrix patch formulation that improved the permeability of the drug and significantly reduces the skin irritation (col.2, lines 33-36). The composition comprising from 0.1 to 20 % (w/w) of a basic drug and from 0.01 to 15 % (w/w) of organic acid or its salt such as sodium acetate (abstract; col.2, lines 40-60; col.3, lines 9-25, 55-58; examples).

US '157 does not expressly disclose the organic acid in the powder from or the mean diameter of the powder particles.

The reference does not expressly disclose the organic acid in the powder from or the mean diameter of the powder particles.

However, in the examples 1 and 2, the reference disclosed the components are hot melted, i.e. not dissolved, and this suggests the powder form of the sodium acetate. Further the reference disclosed in the same examples that the thickness of the adhesive film that contains the components is 100 micrometers, and this implies that the particles size of the powdered organic acid cannot be more than 100 micrometers in diameter.

Thus, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide a transdermal adhesive matrix comprising active agent and sodium acetate powder as disclosed by US '157, and select the sodium acetate having particles size less than 100 micrometers as suggested by the reference, motivated by the teaching of the reference that such a composition for the matrix has improved permeability and significantly reduced skin irritation, with reasonable expectation of having transdermal matrix composition with the contained sodium acetate particles having diameters less than 100 micrometers that highly permeates the skin with minimum irritation.

Applicants' arguments

4. Applicant's arguments filed 02/03/2005 have been fully considered but they are not persuasive. Applicants traverse the rejection of claims 1-12 as being unpatentable over any of JP '365, JP '570 and US '157 by arguing that the cited references do not teach the claimed particle diameters as currently amended. No motivation to modify the

teachings of the references to the claimed particle sizes. US '157 teaches the adhesive composition comprising absorption enhancer. The present applicant has clearly identified the effect of organic acid salt powder of the claimed size to bring superior properties such as improving solubility of the drug into the skin as shown by the examples and working examples.

In response to these arguments, the examiner position is that the claims are directed to composition and all the elements of the composition are disclosed by the cited references, basic drug and organic acid salt. The art recognized the suitability of the sodium acetate in increasing the dermal absorbability of active agents. The difference between the cited art and the present invention is the particle sizes, therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to have the claimed composition with a particle diameters of the organic acid salts ranging from 0.1 to 10 micrometers, since it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller* 105 USPQ 233. The cited references suggest the sodium acetate in the powder form as they all teach dissolving all the other components except for the sodium acetate that is dispersed in the mixture, JP '365 at page 7, paragraph 0030; JP '570 at page 5, paragraph 0020; US '157 at col.11, lines 61-64 and col.12, lines 16-19. The cited references all teach the ion pair formation between the drug and the organic acid salts, JP '365 at page 3, paragraph 009; JP '570 at page 1, paragraph 0004; US '157 at col.2, lines 10-11. Sodium acetate is a known as powder; see the "Condensed Medial Dictionary", page

1007, 1008. It is known to one having ordinary skill in the art that the smaller the particle sizes the easier and more enhanced its transdermal absorption.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, motivation would arise from the teaching of all the references that the ion pairing of the base drug and organic acid salt provides high skin permeation rate and reduced skin irritation. In considering the disclosure of the reference, it is proper to take into account not only the specific teachings of the reference but also the inferences which one skilled in the art would reasonably be expected to draw therefrom. *In re Preda*, 401 F.2d 825, 826, 159 USPQ 342, 344 (CCPA 1968). The rational to modify or to combine the prior art does not have to be expressly stated in the prior art; the rational may be expressly or impliedly contained in the prior art or it may be reasoned from knowledge generally available to one of ordinary skill in the art. The reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve different problem. It is not necessary that the prior art suggest the combination or modification to achieve the same advantage or result discovered by applicant. *In re Linter*, 458 F.2d 1013, 173 USPQ 560 (CCPA 1972).

With regard to the superior results provided by applicants' examples and comparative examples, and with careful review, the examiner has noticed that applicant did not show the effect of particle size at the upper and lower limits of the claimed range, i.e. particle diameter at 0.1 and at 10 micrometer. The comparative examples of record used particle sizes 535 which are the un-grounded sodium acetate. Furthermore, all the examples use only specific organic acid salt, i.e. sodium acetate, and it is not clear if other organic salts will have the same particle sizes and same effect on the precutaneous absorption of the drugs. The examples further contain other ingredients that significantly affect the percutaneous absorption of active agents, such as liquid paraffin, lauryl alcohol and propylene glycol. Therefore, no superior effect has been shown on the percutaneous absorption of base drug that ion paired with organic salt, without the influence of other ingredients.

Conclusion

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Isis Ghali whose telephone number is (571) 272-0595. The examiner can normally be reached on Monday-Thursday, 7:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Isis Ghali
Examiner
Art Unit 1615

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